EP-1266

Acute health-related quality of life changes after liver stereotactic ablative radiotherapy

H. Chung[1], J. Helou[1], I. Thibault[1], W. Chu[1], D. Erler[1], K. Chan[1], E. Chow[1], R. Korol[1], M. Davidson[1], L. Zhang[1]
[1]*Odette Cancer Centre - Sunnybrook Health Science, Radiation Oncology, Toronto, Canada*

Purpose or Objective: Stereotactic ablative radiotherapy (SABR) for liver metastases is currently accepted as a standard treatment option for patients with liver metastases. Multiple studies have demonstrated high rates of local control and low risk of serious toxicities. However, there is limited prospective patient-reported health-related quality of life data (HRQoL). Herein, we report the acute HRQoL changes in patients treated with SABR for liver metastases.

Material and Methods: A prospective study was performed to measure HRQoL changes in patients treated with SABR to 1-3 hepatic metastases. Doses of 30- 60 Gy in 3-5 fractions were delivered as per institutional policy depending on tumor location, histology and size. Changes in patients' self-reported HRQoL were measured using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire–Core 15 Palliative (C15) at baseline (T0) and first follow-up (T1: 6 - 8 weeks post-SABR). The C15 consists of 15 questions; 2 multi-item symptom scales along with 5 single item symptom scales and a final overall QoL question. A significant change in HRQoL was defined as [T0 score-T1 score] > 0.5SD, where SD was the standard deviation of baseline values for each scale. For the overall QoL question, a significant change was defined by a 10-point or greater change from baseline.

Results: Fifty patients were included. Median age at treatment was 65 (40-88) years. Median BED10 was 98 Gy. The 4 most common primary sites of cancer were: gastro-intestinal (29), breast (9), renal cell (4) and lung (4). All patients were Child-Pugh score A. Nine patients had previous hepatectomies for liver metastases. Thirty-one patients had oligometastatic disease≤5(metastases) and 19 had oligoprogression ⩽5 metastases progressing). Forty -seven patients filled the C15 at T1 (94%). The majority of patients did not report a significant change in any of the C15 scales (table 1). For the overall QoL, 64% of the patients reported no significant change at T1, 24% had deterioration and 13% had an improvement.

	Significant Change from Baseline		
C15 Scales	No Significant Change	Improved	Worsen
Physical Functioning	32 (68.09%)	7 (14.89%)	8 (17.02%)
Emotional Functioning	31 (65.96%)	8 (17.02%)	8 (17.02%)
Overall QOL	16 (34.04%)	6 (12.77%)	25 (53.19%)
Pain	18 (38.30%)	16 (34.04%)	13 (27.66%)
Fatigue	26 (55.32%)	7 (14.89%)	14 (29.79%)
Nausea / Vomiting	38 (80.85%)	3 (6.38%)	6 (12.77%)
Appetite loss	34 (72.34%)	6 (12.77%)	7 (14.89%)
Dyspnoea	33 (70.21%)	8 (17.02%)	6 (12.77%)
Insomnia	22 (46.81%)	18 (38.30%)	7 (14.89%)
Constipation	33 (70.21%)	6 (12.77%)	8 (17.02%)
Specific Q7 Scale	30 (63.83%)	6 (12.77%)	11 (23.40%)

Conclusion: SABR offers a non-invasive option for liver metastases ablation. Acute patient-reported outcomes, as measured by C-15, for patients with liver metastases treated with SABR seem favourable. Longer follow-up is needed.

EP-1267

Induction chemotherapy followed by chemoradiotherapy in locally advanced pancreatic adenocarcinoma

J. Reure[1], J. Doyen[1], A. Falk[1], D. Lam Cham Kee[1], L. Evesque[1], P. Follana[1], E. François[1], K. Benezery[1]
[1]*Centre Antoine Lacassagne, Radiotherapy, Nice, France*

Purpose or Objective: Treating locally advanced pancreatic cancer (LAPC) remains a challenging issue. Chemotherapy or chemoradiotherapy alone have not demonstrated their efficacy. A strategy combining chemotherapy and chemoradiotherapy seems promising. Our retrospective analysis aims to evaluate effectiveness and tolerability of induction chemotherapy with Folfirinox followed by chemoradiotherapy in patients with LAPC.

Material and Methods: Nineteen patients treated for LAPC between Mars 2010 and February 2015 were retrospectively identified. These patients with unresectable disease, were initially treated with Folfirinox and then received a chemoradiotherapy with capecitabine or gemcitabine in case of stable disease. Survival was estimated with Kaplan Meier method.

Results: Median number of cycles achieved for Folfirinox was 5. Following chemotherapy, all patients had stable disease and received chemoradiotherapy with capecitabine (53%) or gemcitabine (47%). Majority of patients (63%) received radiotherapy at a dose of 50.4 Gray in 28 fractions. Toxicities are acceptable: three cases of grade 3 nausea / vomiting, three cases of grade 3 asthenia and three cases of grade 3 diarrhea were described during chemotherapy. No grade 3 toxicity was identified during chemoradiotherapy. The median follow-up time was 9 months (1-43 months). Survival rates were 93.8% at six months, 52.7% at 1 year and 21.1% at 2 years. Disease free survival rates were 35.3% at six months, 7.8% at 1 year and 0% at 2 years. Local recurrence free survival rates were 75.3% at six months, 47.3% at 1 year and 31.6 at 2 years. Distant recurrence free survival rates were 34.3% at six months, 18.3% at 1 year and 9.2% at 2 years. At the end of the therapeutic procedure, one patient received surgical resection.

Conclusion: Induction chemotherapy with Folfirinox followed by chemoradiotherapy in locally advanced pancreatic adenocarcinoma seems effective and allows very promising overall and progression free survival rates. Larger studies would be needed to conclusively confirm these observations.

EP-1268

Dosimetric parameters predict toxicity in chemoradiotherapy with nelfinavir for pancreatic cancer

D. Holyoake[1], J. Wilson[1], M. Partridge[2], T. Brunner[3], S. Mukherjee[4], M. Hawkins[1]
[1]*CRUK/MRC Oxford Institute for Radiation Oncology, Advanced Radiation Oncology Group, Oxford, United Kingdom*
[2]*CRUK/MRC Oxford Institute for Radiation Oncology, Radiotherapy Physics Research Group, Oxford, United Kingdom*
[3]*University of Freiburg, Department of Radiation Oncology, Freiburg, Germany*
[4]*Oxford University Hospitals NHS Foundation Trust, Department of Clinical Oncology, Oxford, United Kingdom*

Purpose or Objective: Gastrointestinal (GI) toxicity impedes dose escalation in radiotherapy for pancreatic cancer and limits local tumour control. Clinical data on tolerance doses for the organs of the proximal digestive system remain sparse. We analysed patterns of toxicity in patients treated with concomitant chemoradiotherapy (gemcitabine and cisplatin) with nelfinavir (hypoxia modifier) to identify associated dosimetric factors and establish predictive cut-off values to inform radiotherapy planning.

Material and Methods: Dose-volumes and acute toxicity data were analysed for 21 patients treated for locally-advanced pancreatic cancer in a prospective phase II clinical trial (ARCII, EudraCT 2008-006302-42). Radiotherapy comprised 50.4Gy in 28 daily fractions to the tumour and elective lymph nodes followed by a sequential boost to the primary tumour of 9Gy in 5#. Univariate analysis was performed to investigate association of the dose-volume received by stomach and duodenum with RTOG upper GI toxicity symptoms, and of small-bowel with diarrhoea. Receiver Operating Characteristic analysis was used to identify

strongest predictive factors and to derive optimum cut-off values for predicting likelihood of toxicity incidence.

Results: Grade ≥2 acute RTOG upper GI toxicity attributed to treatment was seen in 11 patients (52%), grade ≥3 in 3 (14%); grade ≥2 diarrhoea was recorded in 3 patients (14%), grade ≥3 in 2 (10%). In patients who experienced grade ≥2 toxicity, stomach V15-55 Gy (absolute volume of stomach receiving 15-55 Gy, in cm3) were significantly larger when compared to those without ($p<0.05$, Mann-Whitney). Differences in V35 Gy and V40 Gy remained significant after Bonferroni correction ($p<0.004$) and ROC analysis was performed to identify the most predictive cut-off values: V35 Gy 55.7cm3 and V40 Gy 43.6 cm3 (both sensitivity 0.82, specificity 0.80, Youden index = 0.62). Significant associations were not seen between duodenal dose-volume and acute toxicity, nor between small-bowel dose-volume and incidence of treatment-related diarrhoea.

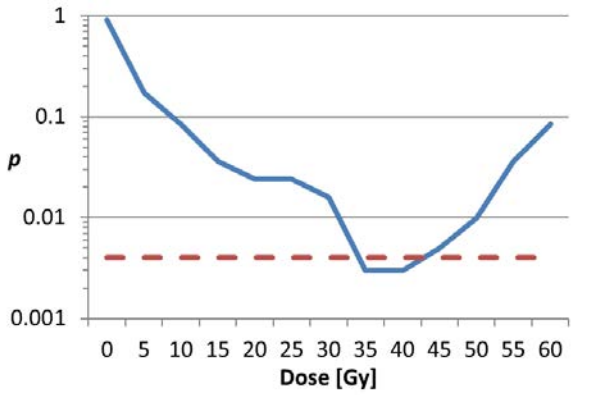

Figure. Results of Mann-Whitney comparison of stomach dose-volume according to grade ≥2 toxicity, showing that $V_{35\,Gy}$ & $V_{40\,Gy}$ are statistically significant predictors

Conclusion: In concomitant chemoradiotherapy with nelfinavir for pancreatic cancer, stomach dosimetric parameters were associated with clinically important acute radiotherapy toxicity and thresholds were derived for predicting toxicity risk. Stomach V35 Gy and V40 Gy were most strongly predictive of acute grade ≥2 side effects.

EP-1269

Dose tolerance of small bowel in patients treated with radiochemotherapy for pancreatic cancer

L. De Filippo[1], G.C. Mattiucci[1], N. Dinapoli[1], M. Boccardi[2], V. Pollutri[1], M. Bianchi[1], R. Canna[1], S. Chiesa[1], G. Macchia[2], A. Morganti[3], V. Valentini[1]

[1]*Università Cattolica del Sacro Cuore -Policlinico A. Gemelli, Radiotherapy Division, Rome, Italy*

[2]*Fondazione di Ricerca e Cura Giovanni Paolo II-Università Cattolica S. Cuore, Department of Radiotherapy, Campobasso, Italy*

[3]*Department of Experimental- Diagnostic and Specialty Medicine - DIMES - University of Bologna- S.Orsola-Malpighi Hospital, Radiation Oncology Unit, Bologna, Italy*

Purpose or Objective: Tolerance of small bowel is the dose limiting factor in radiation therapy for abdominal neoplasms. Bowel constraints for treatment planning in abdominal radiotherapy derive from scientific publications of pelvic tumors. This study has the aim to evaluate dose tolerance of small bowel detecting acute toxicities in patients with pancreatic cancer treated with radiochemotherapy.

Material and Methods: Patients with pancreatic cancer were treated between 2009 and 2014 with 3D-conformal radiotherapy with a total dose of 5040 cGy and conventional fractionation. Chemotherapy with gemcitabine or fluoropyrimidine was simultaneously administered. Nausea, vomit and loss of weight, as acute upper gastrointestinal (GI) toxicities, were scheduled using RTOG scale. In all patients small bowel loops and bowel sac were contoured using QUANTEC guidelines and DVHs were analyzed for this structures using R statistical software (http://www.R-project.org).

Results: Forty-three patients with a median age of 66 years (range 42-79), 14 resected and 29 unresected, were analyzed. Fourteen (32%) patients reported no upper GI toxicity; on 8 (19%), 12 (28%) and 9 (21%) patients were observed respectively grade 1, 2 and 3 toxicity. No grade 4 toxicity was recorded. Nineteen patients discontinued radiotherapy but all of them completed the treatment. Analyzing V Dose on DVHs by logistic regression, small bowel loops V36 Gy resulted as the parameter which most influenced upper GI G1 or higher Toxicity ($p<0.05$). Multivariate analysis showed no impact of surgery on upper GI toxicity.

Conclusion: Our preliminary analysis suggests that new constraints for radiochemotherapy in upper GI cancer could be upgraded. Our study has to be confirmed on a larger sample.

EP-1270

SBRT for liver metastases from low grade neuroendocrine tumors

M. Bignardi[1], A. Huscher[1], M. Centurioni[1], M.M. Colangione[1], D. Barbieri[1], M. Galelli[2], A. Zaniboni[3]

[1]*Fondazione Poliambulanza, Radiation Oncology Unit, Brescia, Italy*

[2]*Fondazione Poliambulanza, Medical Physics, Brescia, Italy*

[3]*Fondazione Poliambulanza, Oncology Department, Brescia, Italy*

Purpose or Objective: Specific results of SBRT for liver metastases from rare tumors have been reported scarcely. This applies also to metastases from low grade neuroendocrine tumors (NET), either derived from gastrointestinal organs or from an unknown primary site. Here we report two cases of multiple liver metastases from low grade NET repeatedly treated by means of SBRT, achieving the outcome of long-term local control.

Material and Methods: From March 2011 to September 2015 49 SBRT courses were delivered to 39 patients for liver metastases from different primaries. All courses were given by VMAT with 6 MV photons, image guided by CBCT in every fraction. Since 2013, deep inspiration breath hold was adopted in order to control organ motion. Two patient had metastases from well differentiated neuroendocrine tumors, one from an unknown primary (patient A), the other from a pancreatic primary (patient B). Patient A underwent two SBRT courses, both in 2011, the first one on segment 6 (CTV volume 25 ml, CTV dose 75 Gy, PTV 50 Gy, in 3 fractions), the second one on two adjacent metastases, respectively in segment 7 and 8 (total CTV volume 54 ml, CTV dose 60 Gy, PTV 50 Gy, in 3 fractions).Patient B received three courses, respectively in 2013, 2014 and 2015. The first SBRT was delivered on segment 6 (CTV volume 38 ml, CTV dose 50 Gy, PTvV45 Gy, in 5 fractions), the second on segment 8 (CTV volume 30 ml, CTV dose 50 Gy, PTV 45 Gy, in 5 fractions), the last on segment 4 (CTV volume 44 ml, CTV dose 50 Gy, PTV 45 Gy, in 5 fractions). Patient A was found to be somatostatine receptor-negative, thus he was followed up mainly by serial CT scans; also, his disease status matched well to trends of two biomarkers (chromogranin A and gastrin). Patient B was followed up by alternating CT scans and PET/CT-68Ga-DOTATOC.

Results: At last follow up patient A achieved long-term local control in S6 metastasis (45 months) as well as in S7-8 (42 months), while showing disease progression at a new liver site at 45 months after first SBRT. At last follow up patient B achieved local control in all sites (S6: 30 months; S8: 13 months; S4: 6 months) with a durable partial PET response in S8 and S4 and a complete PET response in S6. Disease progression took place in two bone sites at 30 months after first SBRT, without any concomitant liver progression.